

MAINE HEALTH ALERT NETWORK

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*****ADVISORY – Important Information*****

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TO: All HAN Recipients

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SUBJECT: Treatment and Prophylaxis with Antivirals for Uninsured and Underinsured Inpatients and Outpatients

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**TREATMENT AND PROPHYLAXIS WITH ANTIVIRALS
MAINE STATE STOCKPILE AVAILABLE FOR UNINSURED AND
UNDERINSURED OUTPATIENTS AS WELL AS INPATIENTS
OCTOBER 31, 2009**

With H1N1 increasingly becoming widespread in Maine, with the disease expected to continue to expand and worsen, and with very limited vaccine supplies, it is critical that health care providers know the importance of **treating and providing prophylaxis for those patients at high-risk for complications with antiviral medicines.** A significant portion of the state stockpile has been available to inpatients for several months, and has now also been distributed for outpatients who do not have adequate insurance covering these medicines. It is important that people at risk for complications from influenza with symptoms or exposure have easy access to antiviral medications, especially since vaccine is in such short supply. This health advisory provides information on accessing the stockpile and the **importance of treatment and prophylaxis with antiviral medications.**

More information may be obtained on both of these topics at:

Accessing Maine's Antiviral Stockpile:

<http://www.maine.gov/dhhs/boh/maineflu/h1n1/anti-viral.shtml>

US CDC Antiviral Guidelines:

<http://www.cdc.gov/h1n1flu/antivirals/>

ACCESS TO MAINE'S ANTIVIRAL STOCKPILE:

Maine's stockpile of antiviral medications (oseltamivir = Tamiflu and zanamivir = Relenza) has been available to hospital patients who are uninsured or under-insured for several months. We have now distributed some additional antiviral medications for use in outpatient settings for those without adequate insurance coverage for the medications. This stockpile is available at Federally Qualified Health Centers (FQHCs), Hannaford pharmacies, hospitals, and other willing pharmacies.

How do I prescribe antiviral medications for someone without adequate insurance coverage?

A prescribing health care provider needs to state on the prescription, "Fill from Maine State Antiviral Cache", and the prescription needs to be presented to either an FQHC, a participating pharmacy, or a willing hospital pharmacy.

Who qualifies for access to the stockpile?

The patient must not have insurance that adequately covers the cost of the medications and must be in a high-risk category for complications from influenza. For instance, these criteria apply to: patients without insurance coverage or with high deductibles or co-pays and insufficient funds to pay. They must also have symptoms that meet the criteria of novel H1N1 infection or have been exposed to a close contact (eg household member) who meets the criteria for novel H1N1. We want to make sure that costs and other factors are not a barrier to accessing antiviral medicines. Further details on accessing the

stockpile are available at: <http://www.maine.gov/dhhs/boh/maineflu/h1n1/anti-viral.shtml>

What do I need to do to track and report the prescribing of antiviral medications from the stockpile?

Health care providers prescribing for the cache must track these prescriptions using the tracking document and fax it by the close of business each Wednesday to Joe Legee at 207-287-4612.

How do I know which pharmacies are participating?

A map listing the participating health centers, Hannaford pharmacies and other locations is available at: <http://www.maine.gov/dhhs/boh/maineflu/h1n1/anti-viral.shtml>

Whom can I talk with about questions?

- Questions about the clinical appropriateness of antiviral medications can be obtained through the Maine CDC's toll-free 24 hour clinical consultation line at: 1-800-821-5821.
- Questions about accessing the stockpile may be directed to the Northern New England Poison Center, toll free 24 hours at 1-800-221-1222.

USE OF ANTIVIRAL MEDICATIONS

It is especially important with the expected continued spread and worsening of H1N1 in Maine with very limited access to vaccine, that antiviral medications be used to reduce the severity and duration of influenza illness as well as reduce the risk of influenza-related complications including severe illness and death.

US CDC Antiviral Guidelines:

<http://www.cdc.gov/h1n1flu/antivirals/>

WHO SHOULD GET ANTIVIRAL MEDICINES?

- **Healthy people with severe symptoms:** Most healthy persons who develop an illness consistent with uncomplicated influenza, or persons who appear to be recovering from influenza, do not need antiviral medications for treatment or prophylaxis. However, persons presenting with suspected influenza and more severe symptoms such as evidence of lower respiratory tract infection or clinical deterioration should receive prompt empiric antiviral therapy, regardless of previous health or age.
- **Hospitalized Patients:** Treatment with oseltamivir (Tamiflu) or zanamivir (Relenza) is recommended for **all persons with suspected or confirmed influenza requiring hospitalization.**
- **Antiviral Priority Groups:** Early empiric treatment with oseltamivir (Tamiflu) or zanamivir (Relenza) should be considered for persons with **suspected or confirmed influenza** who are at higher risk for complications including:
 - **Children younger than 2 years old;**
 - **Persons aged 65 years or older;**

- **Pregnant women and women up to 2 weeks postpartum (including following pregnancy loss);**
- **Persons younger than 19 years of age who are receiving long-term aspirin therapy; and**
- **Persons of any age with certain chronic medical or immunosuppressive conditions:**
 - Chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological (including sickle cell disease), or metabolic disorders (including diabetes mellitus);
 - Disorders that can compromise respiratory function or the handling of respiratory secretions or that can increase the risk for aspiration (e.g., cognitive dysfunction, spinal cord injuries, seizure disorders, or other neuromuscular disorders)
 - Immunosuppression, including that caused by medications or by HIV.
- **Vaccine Priority Groups vs. Antiviral Priority Groups:** Notice the priority groups for antiviral medicines overlap but are not identical to the high priority groups for novel H1N1 vaccine. Priority groups for the vaccine are:
 - Pregnant women
 - All people 6 months – 25 years old
 - Caregivers and household contacts of those under 6 months
 - People with underlying conditions 25 – 64 years of age
 - Health care workers.
- **Why are seniors on the list for antiviral medications but not for vaccine?**
Persons 65 years and older are less likely to become ill with 2009 H1N1 influenza compared to younger persons, since they seem to have some underlying immunity. Therefore, they are not on the high priority list for vaccine. However, when persons aged 65 years or older acquire influenza, they are at higher risk for severe influenza-related complications.

DO NOT DELAY TREATMENT WITH ANTIVIRAL MEDICINES.

- Treatment, when indicated, should be initiated as early as possible because the benefits are greatest when started within the first 2 days of illness. However, some studies of hospitalized patients with seasonal and 2009 H1N1 influenza have suggested benefit of antiviral treatment even when treatment was started more than 48 hours after illness onset.
- **To reduce delays in treatment initiation, consider:**
 - Informing persons at higher risk for influenza complications of signs and symptoms of influenza and need for early treatment after onset of symptoms of influenza (i.e., fever, respiratory symptoms);
 - Ensuring rapid access to telephone consultation and clinical evaluation for these patients as well as patients who report severe illness;
 - Considering empiric treatment of patients at higher risk for influenza complications based on telephone contact if hospitalization is not

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indicated and if this will substantially reduce delay before treatment is initiated.

- Treatment should not wait for laboratory confirmation of influenza because laboratory testing can delay treatment and because a negative rapid test for influenza does not rule out influenza.
- Testing for 2009 H1N1 influenza infection with real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) should be prioritized for persons with suspected or confirmed influenza requiring hospitalization or associated with an institutional outbreak with the need for confirmation.

CHILDREN AND ANTIVIRAL MEDICINES

- Hospitalization rates among children <18 years of age are higher than for adults, and the rates are higher the younger the child. Hospitalization rates for children are about twice that of adults, and 4 times higher than adults for children 2 – 4 years of age.
- Information on the dose and dosing schedule for oseltamivir and zanamivir is provided in this document. An April 2009 Emergency Use Authorization authorizes the emergency use of oseltamivir in children younger than 1 year old (<http://www.cdc.gov/h1n1flu/eua/>), subject to the terms and conditions of the EUA.
- Special Considerations for Children
Aspirin or aspirin-containing products (e.g. bismuth subsalicylate – Pepto Bismol) should not be administered to any confirmed or suspected ill case of influenza aged 18 years old and younger due to the risk of Reye syndrome. For relief of fever, other anti-pyretic medications such as acetaminophen or non-steroidal anti-inflammatory drugs are recommended.
- Children younger than 4 years of age should not be given [over-the-counter cold medications](#) without first speaking with a healthcare provider*.

PREGNANT WOMEN AND ANTIVIRAL MEDICINES

- **Importance of Providing Antiviral Medicines for Pregnant Women:** Pregnant women are known to be at higher risk for complications from infection with seasonal influenza viruses, and severe disease among pregnant women was reported during past pandemics. Hospitalizations and deaths have been reported among pregnant women with 2009 H1N1 influenza virus infection, and one study estimated that the risk for hospitalization for 2009 H1N1 influenza was four times higher for pregnant women than for the general population. While oseltamivir and zanamivir are "Pregnancy Category C" medications, indicating that no clinical studies have been conducted to assess the safety of these medications for pregnant women, the available risk-benefit data indicate pregnant women with suspected or confirmed influenza should receive prompt antiviral therapy. Pregnancy should not be considered a contraindication to oseltamivir or zanamivir use. Because of its systemic activity, oseltamivir is preferred for treatment of pregnant women. The drug of choice for chemoprophylaxis is less clear. Zanamivir may be

preferable because of its limited systemic absorption; however, respiratory complications that may be associated with zanamivir because of its inhaled route of administration need to be considered, especially in women at risk for respiratory problems.

- **Postpartum women:** Anecdotal reports suggest that postpartum women, similar to pregnant women, might be at increased risk for severe complications and death from 2009 H1N1 influenza. These reports are consistent with the postpartum period being a time of transition to normal immune, cardiac, and respiratory function, a transition that is believed to occur quickly, but would be unlikely to occur immediately at delivery. Based on these reports, women should be considered to be at increased risk of influenza-related complications up to 2 weeks postpartum (including following pregnancy loss). Prompt empiric antiviral treatment is indicated for suspected or confirmed 2009 H1N1 influenza in women who are up to 2 weeks postpartum (including following pregnancy loss).

POST EXPOSURE PROPHYLAXIS:

- Consideration for antiviral chemoprophylaxis should generally be reserved for persons at higher risk for influenza-related complications who have had contact with someone likely to have been infected with influenza. However, early treatment is an emphasized alternative to chemoprophylaxis after a suspected exposure. Household or close contacts (with risk factors for influenza complications) of confirmed or suspected cases can be counseled about the early signs and symptoms of influenza, and advised to immediately contact their healthcare provider for evaluation and possible early treatment if clinical signs or symptoms develop. Early recognition of illness and treatment when indicated is preferred to chemoprophylaxis for vaccinated persons after a suspected exposure.
- *Close contact, for the purposes of this document*, is defined as having cared for or lived with a person who is a confirmed, probable, or suspected case of influenza, or having been in a setting where there was a high likelihood of contact with respiratory droplets and/or body fluids of such a person. Examples of close contact include sharing eating or drinking utensils, physical examination, or any other contact between persons likely to result in exposure to respiratory droplets. Close contact typically does not include activities such as walking by an infected person.
- **Post exposure antiviral chemoprophylaxis with either oseltamivir or zanamivir can be considered for the following:**
 - Persons who are at higher risk for complications of influenza and are a close contact of a person with confirmed, probable, or suspected 2009 H1N1 or seasonal influenza during that person's infectious period.
 - Healthcare personnel, public health workers, or first responders who have had a recognized, unprotected close contact exposure to a person with confirmed, probable, or suspected 2009 H1N1 or seasonal influenza during that person's infectious period. Information on appropriate personal protective equipment is available at: [Infection Control for Patients in a](#)

Healthcare Setting and might be updated frequently as additional information on transmission becomes available.

- Antiviral agents should not be used for post exposure chemoprophylaxis in healthy children or adults based on potential exposures in the community, school, camp or other settings.
- Chemoprophylaxis generally is not recommended if more than 48 hours have elapsed since the last contact with an infectious person.
- Chemoprophylaxis is not indicated when contact occurred before or after, but not during, the ill person's infectious period as defined above.
- Persons at ongoing occupational risk for exposure (e.g., healthcare personnel, public health workers, or first responders who are working in communities with influenza outbreaks) should carefully follow guidelines for appropriate personal protective equipment. Efforts to reduce the risk of exposure or infection for healthcare personnel should include appropriate administrative controls (e.g. having healthcare personnel stay home from work when ill, and triaging for identification of potentially infectious patients), cough and hand hygiene, personal protective equipment, and vaccination when available.

INTRAVENOUS ANTIVIRALS

- **EUA on Peramivir IV:** Because the FDA has no intravenous formulation of antiviral product for the treatment of hospitalized patients with influenza, it has issued an Emergency Use Authorization of Peramivir IV (<http://www.cdc.gov/h1n1flu/eua/peramivir.htm>). Peramivir IV is currently under development for treatment of acute influenza in patients who require hospitalization due to the severity of influenza virus infection. The efficacy and safety of Peramivir have not yet been established. For more information: <http://emergency.cdc.gov/h1n1antivirals/>

Additional information about these recommendations can be found in [Questions and Answers: Revised Recommendations for the Use of Influenza Antiviral Drugs](#).

DOSEAGES OF ANTIVIRAL MEDICINES

Table 1. Antiviral medication dosing recommendations for treatment or chemoprophylaxis of 2009 H1N1 infection. (Table extracted from product information for Tamiflu® and Relenza®)			
Medication		Treatment (5 days)	Chemoprophylaxis (10 days)
Oseltamivir			
Adults			
		75-mg capsule twice per day	75-mg capsule once per day
Children ≥ 12 months			
Body Weight (kg)	Body Weight (lbs)		
≤15 kg	≤33lbs	30 mg twice daily	30 mg once per day
> 15 kg to 23 kg	>33 lbs to 51 lbs	45 mg twice daily	45 mg once per day
>23 kg to 40 kg	>51 lbs to 88 lbs	60 mg twice daily	60 mg once per day
>40 kg	>88 lbs	75 mg twice daily	75 mg once per day
Zanamivir			
Adults			
		10 mg (two 5-mg inhalations) twice daily	10 mg (two 5-mg inhalations) once daily
Children (≥7 years or older for treatment, ≥5 years for chemoprophylaxis)			
		10 mg (two 5-mg inhalations) twice daily	10 mg (two 5-mg inhalations) once daily

Healthcare providers and pharmacists should be aware that an oral dosing dispenser with 30 mg, 45 mg, and 60 mg graduations is provided with TAMIFLU® for Oral Suspension, rather than graduations in milliliters (mL) or teaspoons (tsp). There have been cases where the units of measure on the prescription instructions (mL, tsp) do not match the units on the dosing device (mg), which has lead to patient or caregiver confusion and dosing errors. When dispensing commercially manufactured TAMIFLU® for Oral Suspension, pharmacists should ensure the units of measure on the prescription instructions match the dosing device. If prescription instructions specify administration using milliliters (mL) or teaspoons (tsp), then the device included in the Tamiflu® product package should be removed and replaced with an appropriate measuring device, such as an oral syringe if the prescribed dose is in milliliters (mL).

Treatment and Chemoprophylaxis for Children younger than 1 Year of Age
 Children younger than 1 year of age are at higher risk for influenza-related complications and have a higher rate of hospitalization compared to older children. Oseltamivir is not approved for use in children younger than 1 year of age. However, limited safety data on oseltamivir treatment of seasonal influenza in children younger than 1 year of age suggest that severe adverse events are rare. Oseltamivir is authorized for emergency use in children younger than 1 year of age under an EUA issued by FDA, subject to the terms and conditions of the EUA.

Because infants experience high rates of morbidity and mortality from influenza, infants with 2009 H1N1 influenza virus infections may benefit from treatment using oseltamivir. ([Table 2](#) and [Emergency Use Authorization of Tamiflu \(oseltamivir\)](#)).

Table 2. Dosing recommendations for antiviral treatment or chemoprophylaxis of children younger than 1 year using oseltamivir.		
Age	Recommended treatment dose for 5 days	Recommended prophylaxis dose for 10 days
Younger than 3 months	12 mg twice daily	Not recommended unless situation judged critical due to limited data on use in this age group
3-5 months	20 mg twice daily	20 mg once daily
6-11 months	25 mg twice daily	25 mg once daily

Note to Prescribers: When commercially-manufactured Tamiflu® oral suspension is not available, oseltamivir 75 mg capsules can also be compounded at most retail pharmacies into a suspension. Health care providers can suggest this compounding alternative when writing prescriptions for Tamiflu® oral suspension. The Tamiflu® oral suspension concentration is 12 mg/mL; the compounded suspension concentration is 15 mg/mL. We advise prescribers to specify the concentration (e.g. Tamiflu® oral suspension 12mg/mL) if prescribing in mL or teaspoons, or to prescribe the dose in milligrams (mg).

Note to Pharmacists: When dispensing Tamiflu® oral suspension for children younger than 1 year of age, the oral dosing dispenser that is included in the Tamiflu® package should always be removed as it only provides graduations in 30 mg, 45 mg, and 60 mg. An oral syringe that is capable of accurately measuring the prescribed dose in milliliters (mL) should be provided, and the caregiver counseled on how to administer the prescribed dose accurately with the oral syringe provided. For additional information refer to: http://www.cdc.gov/H1N1flu/pharmacist/pharmacist_info.htm and <http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm183649.htm> 